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THE PHARMACOLOGICAL ASSAY OF THE HEART TONICS.*

FIFTEEN YEARS' EXPERIENCE.

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In the early nineties, the possibility of determining the neutralizing value of antidiphtheric serum toward diphtheria toxin by experiments upon animals was clearly shown by several workers, the method devised by Ehrlich after several years' trial in nearly all parts of the world being finally accepted as the standard method for assaying this serum.

One of us (Houghton) commenced a series of experiments in the autumn of 1894, looking forward to the devising of a suitable method of assay that could be rationally applied for the determination of the value of preparations of the heart tonics. These studies have been continued until the present. During this time several papers have been published (A.M.A., June 9, 1898, and since), calling attention to the method of assay, to the great variation in the potency of these drugs, and to the later results obtained, the last paper in the series being a complete presentation of the subject before the International Congress of Applied Chemistry, London, Eng., May, 1909 (*Lancet*, June 19, 1909).

* Presented at the 1909 meeting of the American Pharmaceutical Association, Aug. 19, 1909.

The method as presented to the American Medical Association June 9, 1898, for the assay of strophanthus preparations, has been employed continuously since, with very slight modification, and may be described briefly as follows:

1. The pharmacological assay of drugs depends upon the biological fact that the functioning of the cellular protoplasm of animal tissue may be altered in degree but not in kind through the use of drugs which unite with one or more constituents of the protoplasm, such union probably being chemical.

2. Certain drugs have an elective affinity for special animal tissue, which affinity can be utilized for measuring the value of such drugs. The reaction between strychnine and nerve tissue is a noteworthy example.

3. The reaction chosen as a measure for determining the activity of a given drug should be the most constant and characteristic observable for such. The heart tonics possess a special affinity for the heart muscle, particularly observable when these drugs are administered to frogs, turtles, etc.

4. The kind of animal chosen for making the observation should be the one in which the reaction is most nearly uniform and clearly discernible. In the writers' experience, frogs weighing about 15 grammes each have been chosen on account of their uniformity and the ease with which they can be obtained. (During the breeding season only male frogs should be employed, as at this time the weight of the females is greatly altered by the contained spawn.)

5. The animals employed for making an assay of the heart tonics should be of the same species, differing as little as possible from one another in weight and other characteristics, such as length of time kept in captivity, sex, etc., in order that the resistance of the several animals employed for making a test shall be as uniform as possible.

6. The animals employed should be kept under identically the same conditions prior to and during the time they are used for test purposes. Food, ventilation, moisture, temperature, etc., are important factors in maintaining uniform conditions of experiment.

7. In making a quantitative assay, the strength of the unknown should be compared with the strength of a standard preparation of the same drug, the assay of both being made at the same time and the conditions of the experiment being precisely the same in both cases.

8. The standard adopted should possess the characteristic action

of an average preparation of a given drug. Such standard may be obtained by mixing equal parts of not less than ten lots of the finished preparation, derived from the same number of lots of crude drug which have been determined to be of first-class quality by physical and botanical examination.

9. The action of the drug being assayed should, if possible, be compared with the action of the standard upon the same animal.

10. In those cases where it is impossible to make an assay using

TABLE I.

OUTLINE OF METHOD OF OBTAINING M. F. D. TINCTURE STROPHANTHUS, U. S. P. 1890.

Weight.	Dose per Gm. body weight.	Total dose 1% sol.	Result.
16 Gms.	.0001	.16	Alive.
15 "	.00015	.23	Alive.
17 "	.0002	.34	Alive.
15 "	.00025	.38	Dead.
16 "	.0002	.32	Alive.
17 "	.00021	.36	Alive.
15 "	.00022	.33	Dead.
16 "	.00023	.37	Dead.
17 "	.00024	.41	Dead.
16 "	.00022	.35	Dead.
17 "	.00022	.37	Dead.
15 "	.00022	.33	Dead.
16 "	.00022	.35	Alive.
17 "	.00022	.37	Alive.
	STANDARD.		
16 "	.00016	.26	Alive.
16 "	.00016	.26	Dead.
16 "	.00016	.26	Dead.
17 "	.00016	.27	Dead.
18 "	.00016	.28	Alive.

Strength of sample is $\frac{.00016}{.00022} = \frac{16}{22}$ of the standard = 72 per cent = 465 + heart tonic units (H. T. U.s) per Cc.

a single animal, a sufficient number of animals of as nearly uniform resistance as possible should be employed to rule out any individual idiosyncrasy. In the testing of the heart tonics upon frogs, this is of great importance.

11. Apparatus required for making assays of the heart tonics. Small wire frog baskets with legs and covers or frog glasses and plates will do, care being taken not to set the baskets too deeply in water and not to fill the plates sufficiently full of water to drown the

animals. The water should cover the bottom of the baskets or plates about one-fourth inch. Small balance for weighing the frogs. Volumetric flasks for diluting the preparations to be assayed, and glass pipettes, graduated into hundredths of a cubic centimetre, with long narrow points, or, better, supplied with hypodermic needle-points for injecting the frogs.

12. The frogs should be handled with much care, avoiding squeezing, pinching, and such while making the injection in the abdominal lymph-sac. The amount of the heart tonic preparation should be very carefully diluted with physiological salt solution, so that the total quantity injected into each frog will be about 0.5 c.c.

13. It is necessary in making an assay of the heart tonics to inject several series of frogs (see Table I).

14. Death of the frog should be the criterion for reading end results, a final examination of the frog being made at the end of twelve hours; those dying prior to the end of the twelve-hour period are considered as killed by the drug, unless some accident has occurred.

15. Ten times the normal minimum fatal dose (M.F.D.) per gramme body weight of frog of the standard preparation properly diluted and injected is considered as a heart tonic unit (H.T.U.), consequently the number of H.T.U.s in a given cubic centimetre of a preparation is one-tenth of the quotient obtained by dividing one by such M.F.D., *i.e.*, the number of H.T.U.s in each cubic centimetre of fluid is one-tenth of the reciprocal of the M.F.D. To illustrate: if the minimum fatal dose of a given drug per gramme body weight of frog is found to be equivalent to 0.01, then the given substance, assuming that it belongs to the group of heart tonics, would contain 10 heart tonic units: $(\text{M.F.D. } \frac{1}{0.01} \div 10 =$ 10 H.T.U,s). This rule can be applied to any of the heart tonics as a means of expressing such values in whole numbers. Definition: A heart tonic unit (H.T.U.) is ten times the normal minimum fatal dose per gramme body weight of standard test frogs kept under proper test conditions.

It is to be understood that the H.T.U. is a measure of toxic value, although such toxic values may be translated directly into therapeutic values, based on the U.S.P. average dose or any other dose.

16. Instead of stating the full number of heart tonic units in all cases, round numbers can be used, which do not vary more than a given per cent. from the actual number of units. Reference to Table II shows what may be accomplished.

In actual practice a table can be constructed similar to the above for all the values that will be derived in the testing of the heart tonics under all conditions. These may be printed on a sheet or sheets of paper and kept for reference in a book form or placed on

TABLE II.

M. F. D. = normal minimum fatal dose per Gm. body weight of Frog.
H. T. U.s = heart tonic units.

M. F. D.	Exact No. H. T. U.s in 1 Cc.	Approximate No. H. T. U. s in 1 Cc.	Per cent. of Error.
.0001	1000	1000	0
.0002	500	500	0
.0003	333	330	1.
.0004	250	250	0
.0005	200	200	0
.0006	166	160	4.
.0007	142	140	2.
.0008	125	125	0
.0009	111	110	.9
.0010	100	100	0
.0011	91	91	0
.0012	83	80	3.
.0013	77	77	0
.0014	71	70	1.
.0015	66	66	0
.0016	62	62	0
.0017	59	59	0
.0018	55	55	0
.0019	53	53	0
.0020	50	50	0
.0100	10	10	0

a chart to hang on the wall of the operation room and used in the same manner as interest or logarithm tables. Such practice would obviate entirely the necessity for the person doing the testing to make mathematical computations unless a correction would be needed, in order to convert an abnormal minimum fatal dose of standard into H.T.U.s as stated below. These variations can also be worked out and converted into tables.

17. A correction will be necessary where the minimum fatal dose of the standard is more or less than that mentioned in the table of proposed standard values, such correction to be made as per illus-

tration already cited, Table I. According to the formula, the minimum fatal dose of standard divided by the minimum fatal dose of unknown

$$\left(\frac{\text{M.F.D. of standard}}{\text{M.F.D. of unknown}} = \text{per cent. unknown is of standard}\right)$$

equals the percentage value of unknown. The percentage value of the unknown can easily be converted into H.T.U.s by multiplying the number of H.T.U.s in standard by the per cent. value.

LOSS IN POTENCY OF PREPARATIONS OF THE HEART TONICS WITH AGE.

A. Preparations of Digitalis.

TABLE III.

LOSS OF POTENCY OF DIGITALIS PREPARATIONS WITH AGE.

Prep.	No. sample.	Av. No. H. T. U.s per Cc. when mfg.	Years later.	Av. No. H. T. U.s	Av. yearly loss %.
Extract 94% Alcohol + 47% Alcohol	11	260	5	160	8%
Fl. Ext. U. S. P. 7th Rev.	8	72	6	55	4%
Fl. Ext. U. S. P. 8th Rev.	11	55	3½	35	10%
Tincture U. S. P. 8th Rev.	8	7	3	5	9%

1. Extract of digitalis made by using 94 per cent. alcohol followed by 47 per cent. alcohol as menstruum.

Average potency of eleven samples at the time of manufacture in round numbers contained 260 H.T.U.s per gramme of extract. Five years later the average strength had fallen to 160 H.T.U.s per gramme—a loss of nearly 40 per cent., or about 8 per cent. each year.

2. Fluidextract digitalis, U.S.P. 7th Rev., 62.7 per cent. alcohol.

Average potency of eight samples at the time of manufacture 720 H.T.U.s per c.c. Six years later the strength had fallen to 550 H.T.U.s per c.c.—a loss of about one-fourth, or 4 per cent. per year.

3. Fluidextract digitalis, U.S.P. 8th Rev., 48 per cent. alcohol.

Average potency of eleven samples at time of manufacture 550

H.T.U.s per c.c. Three and a half years later 358 H.T.U.s. Average loss about 10 per cent. yearly.

A very important point should be noted in this connection, namely, the menstruum adopted in the last U.S.P. for the preparation of fluidextract digitalis is much less desirable than the U.S.P. 7th Revision in at least two respects. Repeated trials show that it is almost impossible to get a finished product containing the full number of H.T.U.s of the standard we had previously adopted, the average being as above stated, 550 H.T.U.s per c.c., while with drug of the same quality when the 7th Revision menstruum is employed no difficulty is experienced. Owing to this it was decided to no longer attempt to assay physiologically the 8th Revision product and to take such statement referring to it off the label, but, in order to supply the medical profession with a full strength fluidextract of the drug, it was decided to prepare such with a menstruum containing a larger per cent. of alcohol which could be assayed and so labelled. In the second place the loss in potency of the 8th Revision is about 10 per cent. per year, while with the 7th Revision it is less than one-half as great, or about 4 per cent. The results coincide quite closely with those following the change made in the menstruum for the fluidextract of squill except that the loss in activity was greater in the latter drug, as pointed out (Houghton in the *J.A.M.A.*, June 12, 1906) three years ago. In this paper several methods of physiological assay showed very clearly that a serious mistake had been made in changing to acetic acid as a menstruum. The writers feel certain that any one who has tried the 8th Revision menstruum for fluidextract digitalis has found that it is much less satisfactory from a pharmaceutical point of view, to say nothing of the loss in potency.

4. Tincture digitalis, U.S.P. 8th Revision, 48.9 per cent. alcohol.

The average strength of six samples was found to be at the time of manufacture 7 H.T.U.s per c.c., while three years later the strength had fallen to 5 H.T.U.s per c.c., or an average yearly loss of 9 per cent. While the number of samples examined may not be sufficient for drawing final conclusions, it seems to us that there is no question about the preparations of digitalis losing strength on standing. The greater the per cent. of alcohol in the menstruum the more stable the product.

The experiments to determine the loss in potency of the preparations of digitalis have not been entirely completed, but the

final results will be published as soon as possible with data relative to the deterioration of the other members of the heart tonic series.

TABLE IV.

POTENCY OF PREPARATIONS OF HEART TONICS AS PURCHASED ON THE OPEN MARKET.

Fluid Extracts of Digitalis.

No. of manufacturer.	H. T. U.s per Cc. U. S. P. 7th Rev.	U. S. P. 8th Rev.
1	33	19
	22	
	33	
2	82	
	56	
3	66	33
4	46	
5	46	
6	66	40
	40	
	66	
7	50	
	88	
	50	
8	33	
	33	
9	88	
10	..	13
11	..	26

Average for 17 samples U. S. P. 7th Rev., 53 H. T. U.s per Cc.
Average for 5 samples U. S. P. 8th Rev., 26 H. T. U.s per Cc.

English Manufacturers.

12	40
13	33
14	53
15	16
16	50
17	33
18	26
19	30
20	26

Average for 9 samples, 34 H. T. U.s per Cc.

Tincture of Digitalis, U. S. P.

Standard 1/10 Potency of F. E. Digitalis.

3	6
2	6

Extract of Digitalis.

Standard 3 Times Potency of F. E. Digitalis.

6	150
	110
2	170

Average, 150 H. T. U.s per Gm.

F. E. Squill.

1	50	
6	20	
3	41	
28	..	12
11	66	

Average for 4 samples, 44 H. T. U.s.

Tincture Strophanthus.

10	...	1200
6	...	1333
22	...	666
1	...	1200
3	400	
		B. P.
23	...	333
14	...	167
24	...	300
15	...	333
25	...	333
26	...	533
13	...	167
27	...	167
1	...	333
6	...	266

Averages, 400, 1100, and B. P. 300 H. T. U.s per Cc.

TABLE V.

ASSAYS OF 12 CONSECUTIVE LOTS OF CRUDE DIGITALIS LEAVES SUBMITTED FOR PURCHASE.

Fluid Extract Made According to 7th Revision, U. S. P.

Per cent of standard.	H. T. U.s per Cc.	Per cent of standard.	H. T. U.s per Cc.
100	66	75	50
80	50	60	40
120	80	70	46
75	50	100	66
125	82	125	82
200	132	75	50

Average for 12 samples, 66

Activity compared with the proposed standard: Minimum fatal dose per Gm., 0.0015 Cc. = 66 H. T. U.s per Cc.

In view of the results we have already obtained, and particularly those regarding the digitalis preparations, we strongly recommend that at the time of manufacture, after proper aging, preparations of digitalis be assayed and a statement be made on the label, stating when the assay was made and the number of H.T.U.s contained per c.c. Such number of H.T.U.s should, of course, be the number selected as of standard potency; in other words, hold the finished product to a standard of uniform activity. It would be very desir-

able for manufacturers in all countries to adopt the same standard, as was recently pointed out and urged by one of us (Houghton, London *Lancet,* June 19, 1909).

A possible explanation for the loss in activity of preparations of digitalis may be that it is due to a ferment which is not destroyed by the menstruum, as pointed out by Rosenthaler and Meyer; or

TABLE VI.

FLUID EXTRACT DIGITALIS, 7TH REVISION.

No.	M. F. D.	Units.
5	.0008	125
3	.0009	125
2	.00095	105
4	.0010	100
4	.0011	91
8	.0012	83
7	.0013	77
8	.0014	71
10	.0015	66
4	.0016	62
2	.0017	58
5	.0018	55
2	.0019	52
6	.0020	50
2	.0021	47
2	.0022	45
1	.0024	41
1	.0027	37
2	.0030	33
1	.0031	32
1	.0032	31
1	.0035	28
1	.0066	15
1	.0075	13

Summary—Fluid Extract Digitalis, 7th Rev.

	M. F. D.	H. T. U.s per Cc.
Standard adopted in 1898	.0015	66
Average for 83 samples tested since 1901	....	70
Proposed standard for 7th Rev. U. S. P.	....	65

again it may well be that these products are acted upon in a detrimental way by the soluble constituents in the glass used in the bottles for storing the material (see "Dictionary of Chemical Solubilities," Comey). Certain it is, American glassware varies a great deal in its composition. This strikingly came to our notice in connection with the use of test-tubes for growing cultures of bacteria. In some instances the glass contained sufficient alkalinity to inhibit the growth of the germs entirely. Indeed it has been a source of con-

siderable trouble in our laboratory for many years, so much so that we have found it necessary to carefully test out each lot of glass tubing before it is used for test-tubes for culture media purposes.

It might be thought on considering Table V, since the results check up so closely with the proposed standard for fluidextract digitalis, that the same figures had been used in both cases. This, however, is not true, as the samples mentioned in Table V were simply worked out in the course of every-day laboratory testing, recorded in a book kept for that purpose, and were taken off, as intimated, consecutively, merely to illustrate the variability in the activity of crude digitalis leaves as they appear on the market.

TABLE VII.

FLUID EXTRACT SQUILL, 7TH REVISION.

No.	M. F. D.	Units.
1	.0006	166
2	.0007	142
6	.0008	125
2	.0009	111
10	.0010	100
7	.0011	91
7	.0012	83
2	.0013	76
4	.0014	71
4	.0015	66
2	.0016	62
1	.0018	55
1	.0019	52
1	.0022	45
2	.0024	41
1	.0025	40
1	.0032	31
1	.0035	28
1	.0038	26
1	.0040	25
2	.0050	20
1	.0056	17
1	.0065	15

Summary—Fluid Extract Squill, U. S. P. 7th Rev.

	M. F. D.	H. T. U.s per Cc.
Standard adopted in 1901	.0012	83
Average for 61 samples	....	80
Proposed standard for 7th Rev. U. S. P	....	80

These figures were derived in a manner similar to that used for the derivation of the minimum fatal dose for the standard tincture of strophanthus, as previously stated. Reference to the following synopses dealing with strophanthus, digitalis, squill, and con-

vallaria shows how accurately these figures correspond with the results obtained in routine practice in a large manufacturing laboratory.

TABLE VIII.

FLUID EXTRACT CONVALLARIA (RHIZOME AND ROOTS), 7TH AND 8TH REVISIONS.

No.	M. F. D.	Units.
2	.00014	714
1	.00015	666
1	.00018	555
2	.00020	500
1	.00021	476
3	.00022	454
5	.00024	416
1	.00025	400
2	.00026	384
1	.00027	370
1	.00029	344
1	.00031	322
1	.00032	312
1	.00033	303
1	.00034	294
1	.00036	277
2	.00039	256
2	.00040	250
1	.00045	222

Summary—Fluid Extract Convallaria: Rhizome and Roots.

	M. F. D.	H. T. U.s per Cc.
Standard adopted in 1900	.00025	400
Average for 30 samples	.....	406
Proposed standard	.....	400

TABLE IX.

5 PER CENT TINCTURE STROPHANTHUS, U. S. P. 1890.

No.	M. F. D.	Units.
11	.00011	909
12	.00012	825
9	.00013	769
11	.00014	714
20	.00015	666
21	.00016	625
7	.00017	588
15	.00020	500
9	.00030	333
11	.00040	250
8	.00050	200

Summary—Tincture of Strophanthus, U. S. P. 1890 (5 per cent).

	M. F. D.	Units.
Standard adopted in 1897	0.00015	666
Average for 134 samples tested since 1901	0.000167	598

Proposed standard U. S. P., 1900, Tr. 10 per cent, 1200 H. T.U.s per Cc. (See also Table VII.)

The averages indicate the actual results obtained on all the samples of the preparations tested since the year 1901. The records for the previous five years were unfortunately destroyed in a fire that we had in our laboratory in 1903, consequently the figures for that period are not available. It should be observed that the figure for the standard tincture of strophanthus was given in the paper pub-

TABLE X.

STANDARD TINCTURE STROPHANTHUS 5 PER CENT., U. S. P. 1890.

M. F. D. Tincture Strophanthus, prepared from samples of drug bought on American market.

1	.00015	8	.00015
2	.00026	9	.00022
3	.00015	10	.00017
4	.00012	11	.00016
5	.00013	12	.00015
6	.00015	13	.00025
7	.00010	14	.00033

(Presented before A. M. A., June, 1898.)

Average M. F. D. = .00017 = 588 H. T. U.s per Cc.
Standard proposed for U. S. P., 7th Revision = 600 H. T. U.s per Cc.
Standard proposed for U. S. P., 8th Revision = 1200 H. T. U.s per Cc.
(See also Table I.)

lished in 1898, and that it closely approximates with those derived from the assay of 134 samples of tincture of strophanthus tested, as stated, since the year 1901.

GENERAL CONCLUSIONS.

It seems to us we are warranted in concluding, since the chemical assay of the heart tonics of the digitalis series has been so thoroughly demonstrated to be unreliable, that some method of pharmacological assay must be adopted in order to safeguard the therapeutic application of these products:

Nearly fifteen years' experience has shown that the method proposed gives reasonably accurate results.

For the fluidextract of digitalis and the fluidextract of squill, U.S.P. 8th Revision, we do not feel warranted at this time in proposing a standard for activity, as we have found that the menstruums proposed for these products do not completely exhaust the drug.

We believe it wise to adopt a heart tonic unit (H.T.U.) which is ten times the normal minimum fatal dose per gramme body weight of standard test frogs kept under proper test conditions.

The standard of physiological activity should be equal to the average value of the given preparation, determined at the season of the year when the most uniform results may be obtained. Best established, as in the case of the standards proposed, by comparison of the results obtained during several years' testing.

TABLE XI.

PROPOSED STANDARDS FOR THE MOST IMPORTANT PREPARATIONS OF THE DIGITALIS SERIES OF THE HEART TONICS.

	M. F. D.	Exact No. of H. T. units per Cc.	No. of H. T. units in round numbers per Cc.
Digitalis—Fluid Extract, U. S. P. 1890...	.0015	66	65
Solid Extract	.0005	200	200
Tincture, U. S. P. 1900.....	.015	6	6
Digitalin (Germanic	.00005	2000	2000
Squill—Fluid Extract U. S. P. 1890.....	.0012	83	80
Strophanthus—Tincture U. S. P. 1900...	.0000833	1200	1200
Convallaria—Fluid Extract:			
Rhizome, and Roots, U. S. P....	.00025	400	400
Herb	.00015	666	650
Flowers	.00009	1111	1100

It is recommended that the number of heart tonic units per cubic centimetre be placed on the label of each preparation at the time it is tested and finished for placing on the market, also the date of manufacture.

The authors realize that it may be possible and desirable with added knowledge as the result of laboratory experiments, to improve the method of assay proposed. It is believed, however, that strict adherence to the method of assay and proper labelling as outlined will result in more uniformly active products of this class, as they appear on the market, and safeguard their therapeutic use.

SOME FURTHER WORK ON FLUIDGLYCERATES.*

By George M. Beringer.

In two previous papers[1] dealing with the subject of fluidglycerates, the writer has given an account of experiments on the extraction of various drugs with glycerol-water menstruums and the preparation of a number of concentrated liquids representing this proposed new class of galenicals.

The manufacture of a few of these fluidglycerates on a moderate scale has been attempted, and the practical use by physicians already indicates that such fluidglycerates as cascara sagrada, chirata, glycyrrhiza, krameria, sumach berries, and sarsaparilla are acceptable preparations, and further efforts will probably demonstrate that this list of useful remedies of this class may be greatly extended.

In a recent communication presented to the New Jersey Pharmaceutical Association,[2] the results of experiments made with the view of studying the application of the principle of glycerol-water extraction to the preparation of syrups are described. It was shown that quite a number of syrups can be thus prepared direct from the drugs without the use of fluidextracts or the introduction of any alcohol. Those for which improved formulas based on this method were presented and samples exhibited included syrups of ipecac, krameria, lactucarium, rhubarb, rose, rubus, compound sarsaparilla, compound squill, senega, and licorice.

In the extensive paper on "Fluidglycerates" presented before this section last year, it was explained that the experiments so far made on the preparation of fluidglycerates of certain drugs were not satisfactory, and further experimentation was intended. Among the refractory drugs so mentioned were nux vomica, red rose, and sanguinaria. Experiments since carried on with these three have resulted in marked improvements. The purpose of the present paper is to communicate improved formulas for these and also to present the results of some experiments upon a few fluidglycerates of a different class of drugs that require for their extraction the use of an alkali in the menstruum.

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* Read at the Section on Practical Pharmacy and Dispensing of the American Pharmaceutical Association, September, 1909.

[1] Proceedings N. J. Phar. Assoc., 1907, p. 56. Proceedings Amer. Pharm. Assoc., 1908, p. 981.

[2] American Journal of Pharmacy, 1909, July, p. 311.

FLUIDGLYCERATE OF NUX VOMICA.—In the earlier experiments on this preparation, acetic acid was added to the menstruum to extract the alkaloids. The resulting product soon thickened and eventually became of a mucilaginous and almost gelatinous consistence. In recent experiments, the acetic acid was displaced by either hydrochloric, sulphuric, or phosphoric acid. The preparation made with phosphoric acid has also thickened and become almost gelatinous, closely resembling that made with acetic acid. The product made with the addition of sulphuric acid has deposited a white precipitate closely adhering to the bottom of the bottle. This sediment proved to be calcium sulphate, the calcium salt evidently present in the drug being extracted and deposited as sulphate. This sediment is readily removed by decanting the supernatant liquid, which is bright, clear, and deep in color and has kept quite limpid for nearly six months, with no sign of any further deposit or thickening. It mixes perfectly clear with water, syrup, or diluted alcohol, but strong alcohol renders it turbid. The average of two assays gave 1.002 strychnine in 100 c.c. The product made with the addition of hydrochloric acid is lighter in color than that containing sulphuric acid and has remained clear and limpid. It likewise mixes clear with water, syrup, or diluted alcohol, and becomes turbid with strong alcohol. The average of three assays was 0.996 strychnine in 100 c.c.

As a result of these experiments the following is submitted as an improved formula for fluidglycerate of nux vomica:

Take of Nux vomica in No. 30 powder	100 Gm.
Hydrochloric acid[3]	5 c.c.
Glycerin	50 c.c.
Water	145 c.c.
Chloroform water, a sufficient quantity.	

Mix the hydrochloric acid with the water and glycerin and moisten the drug with 85 c.c. of the mixture and pack it *lightly* in a percolator. Pour on sufficient of the menstruum to thoroughly saturate the drug and allow to macerate for forty-eight hours. Then percolate slowly, using the balance of the menstruum and then chloroform water till extracted. Reserve the first 50 c.c. of the percolate, concentrate the remainder on a water-bath to 60 c.c., add the

[3] If sulphuric acid is preferred, then use 4 c.c. of sulphuric acid in place of 5 c.c. of the hydrochloric acid directed in the formula.

reserve, and continue the evaporation till the product measures 100 c.c.

FLUIDGLYCERATE OF RED ROSE.—It was intimated in my previous paper that the addition of an acid to the menstruum would possibly improve this preparation. Sulphuric acid seems to fix the color of rose and to be specially indicated in the liquid preparations of that drug. The following is the improved formula for fluidglycerate of rose:

Take of	Red rose in No. 60 powder	100 Gm.
	Diluted sulphuric acid	10 c.c.
	Glycerin	50 c.c.
	Distilled water	140 c.c.
	Chloroform water, a sufficient quantity.	

Mix the acid, glycerin, and water, and having thoroughly mixed the rose with 300 Gm. of clean, pure white sand,[4] moisten it with 80 c.c. of this menstruum and transfer to a percolator, shaking down evenly but not packing. Pour on sufficient of the menstruum to saturate the drug and allow to macerate for forty-eight hours, then percolate slowly, using the remainder of the menstruum and then chloroform water till extracted. Reserve the first 50 c.c. of percolate and evaporate the remainder on the water-bath to 60 c.c., add the reserve, and concentrate to 100 c.c. The product is a deep rich red color, clear, astringent, and with a fine aroma and taste of rose. It mixes perfectly clear with water, syrup, or diluted alcohol, but is coagulated by alcohol. It would make a good basic preparation, as it can be diluted for making a syrup, gargle, or mouth wash where rose is desirable.

FLUIDGLYCERATE OF SANGUINARIA.—This is a difficult drug to extract and represent in a concentrated liquid preparation that will be permanent and active. For some reason, acetic acid has been considered as particularly well adapted for its extraction, and this is evidenced in the official fluidextract and in the formulas for the syrup and vinegar. Quite naturally the writer followed this idea in his experiments, and in the formula submitted last year acetic acid was used but it was stated that the product was not satisfactory, as it

[4] For this purpose sand free from iron is necessary, and the purest commercial white sand obtainable was boiled with diluted hydrochloric acid and then washed by decantation and finally on a strainer till the wash water ceased to give a precipitate with silver nitrate T. S.

had developed considerable sediment and did not mix clear with water or syrup.

Subsequently experiments were made with varying proportions of acetic acid. Somewhat better results were obtained by increasing the acetic acid to 30 c.c. in 100 c.c. of product and using this mixed with 50 c.c. of glycerin and 120 c.c. of water as the first menstruum. But even with this relatively large acid content the product soon became cloudy and deposited considerable sediment, although its miscibility with other liquids was improved. It mixed clear with syrup and diluted alcohol and produced only an opalescence with water, but with alcohol it became turbid.

Since acetic acid did not prove satisfactory, my attention was directed to the use of hydrochloric acid. The experiments indicate that it has decided advantage over acetic acid for extracting this drug and suggest that its use in this connection should be investigated, as it appears to offer an improvement in the formulas for the official preparations of the same.

The following is the improved formula for fluidglycerate of sanguinaria:

Take of Sanguinaria in No. 20 powder	100 Gm.
Hydrochloric acid	10 c.c.
Glycerin	50 c.c.
Water	140 c.c.
Chloroform water, a sufficient quantity.	

Mix the acid, glycerin, and water, and moisten the drug with 50 c.c. of the mixture, transfer to a percolator, and shake down evenly, *without packing,* and pour on sufficient of the menstruum to saturate and allow to macerate for forty-eight hours. Then percolate slowly, using the remainder of the menstruum and then chloroform water till extracted. Reserve the first 50 c.c. of the percolate and evaporate the remainder to 60 c.c., add the reserve, and concentrate to 100 c.c.

This product is clear dark red in color, and after standing three months has shown no tendency to precipitation. It mixes clear with syrup, diluted alcohol, and alcohol, and with water produces a slight opalescence. It possesses the bitter, acrid, and irritating taste of the drug, and the smallest amount tasted produced the disagreeable irritating effect on the mucous surfaces. The physical characteristics of the fluidglycerate so made appear to fully represent the drug

and the marc is free from acridity and is deprived of the red color.

ALKALINE FLUIDGLYCERATES.—There are a number of drugs that require the presence of an alkali for their proper extraction. In the previous paper three fluidglycerates of this class of drugs were considered, namely, fluidglycerates of glycyrrhiza and senega and the bitterless fluidglycerate of cascara. Three more of this class have been investigated since, viz., buchu, eriodictyon, and grindelia, and formulas for these are here given.

FLUIDGLYCERATE OF BUCHU.

Take of Buchu in No. 20 powder	100 Gm.
Solution of potassium hydroxide	50 c.c.
Glycerin	50 c.c.
Water	100 c.c.
Chloroform water, a sufficient quantity.	

Mix the solution of potassium hydroxide, glycerin, and water and moisten the drug with 100 c.c. of this menstruum. Transfer to a percolator and shake down evenly, then pour on sufficient of the menstruum to thoroughly saturate. Allow to macerate for forty-eight hours and then percolate slowly, using the remainder of the menstruum and then chloroform water till extracted. Reserve the first 50 c.c. of the percolate and evaporate the remainder on a water-bath to 60 c.c., add the reserve, and concentrate to 100 c.c. This product is a thick, almost mucilaginous fluid that has deposited no sediment. It possesses the odor and taste of the drug. It mixes clear with syrup and diluted alcohol and opalescent with water, and is coagulated by alcohol.

FLUIDGLYCERATE OF ERIODICTYON.

Take of Eriodictyon in No. 20 powder	100 Gm.
Solution sodium hydroxide	50 c.c.
Glycerin	50 c.c.
Water	100 c.c.
Chloroform water, a sufficient quantity.	

Mix the solution of sodium hydroxide, glycerin, and water and moisten the yerba santa with 80 c.c. of the mixture. Proceed to extract and finish as directed in the formula for fluidglycerate of buchu. The resulting preparation has the color, taste, and odor of yerba santa and has developed only a scant sediment. It mixes

clear with syrup and diluted alcohol, and with water produces only a slight opalescence, but with alcohol a turbid mixture results.

In this preparation sodium hydroxide has been selected because its principal use will be as a disguise for quinine sulphate and other bitter alkaloids and drugs, and sodium sulphate resulting in such mixtures is less apt to crystallize out than if potassium hydroxide was used with potassium sulphate as a resultant. It will serve as a basic preparation for syrup of yerba santa and for admixture with chocolate syrup and similar flavorings and diluents.

FLUIDGLYCERATE OF GRINDELIA.

Take of Grindelia in No. 20 powder	100 Gm.
Solution of potassium hydroxide	50 c.c.
Glycerin	50 c.c.
Water	100 c.c.
Chloroform water, a sufficient quantity.	

Proceed exactly as directed in the formula for fluidglycerate of buchu.

The product is a clear, deep brown colored liquid possessing strongly the odor and taste of grindelia and showing no precipitate. It mixes clear with water, syrup, diluted alcohol, and cloudy with alcohol.

There is already considerable demand for the so-called "aqueous" or "soluble" fluidextract of grindelia as a topical application in rhus poisoning, and this alkaline fluidglycerate will doubtless prove equally as effective for this purpose.

CO-OPERATIVE WORK ON HEADACHE MIXTURES.*

By W. O. Emery.

After making investigations of various suggested methods for determining the different constituents present in the many headache mixtures containing acetanilid and similar agents, a method was finally devised which proved quite satisfactory to the members of the Division of Drugs, and it was therefore decided to place this

* Reprint from the Proceedings of the Twenty-fifth Annual Convention of the Association of Official Agricultural Chemists (1908), Bul. 122, Bureau of Chemistry, U. S. Dept. of Agriculture.

method in the hands of as many chemists interested in this line of work as could assist. A circular letter requesting co-operation was sent out, and a gratifying number responded, signifying their willingness to assist, eleven of whom sent in results. All who expressed a desire to co-operate were supplied with a sample of a mixture containing known amounts of acetanilid, sodium bicarbonate, and caffein, with the following instructions, the U. S. Pharmacopœia, eighth revision, as amended and corrected May 1 and June 1, 1907, being used as a basis for all calculations and reagents unless otherwise specified:

SEPARATION OF CAFFEIN, ACETANILID, AND SODIUM BICARBONATE.

Caffein.

Weigh out about 0.3 Gm. of headache powder on a small (5.5 cm.) tared filter,[1] wash with successive small portions of chloroform to the amount of about 30 c.c., collecting the solvent in a 100 c.c. Erlenmeyer. Distil off chloroform by means of a small flame until only a few cubic centimetres remain. Add 10 c.c. of dilute sulphuric acid, then continue the distillation till all the chloroform has gone over, disconnect from condenser, heat gently, first on wire gauze to complete solution,[2] finally on a steam or hot-water bath until the contents of the flask have evaporated to about 3 to 4 c.c. Cool, transfer by washing with water to a separatory funnel, so that the final volume does not greatly exceed 20 c.c. Add four times the volume, or about 80 c.c. of chloroform, shake for some time vigorously, allow to stand until the chloroform clears perfectly, pass through a small dry filter into a dry 100 c.c. Erlenmeyer, distil off the solvent, and use distillate for a second extraction, observing the same method of shaking, clearing, and filtering as above noted. Distil off chloroform to a small volume, transfer residue to a small tared beaker or crystallizing dish by means of a few cubic centimetres of chloroform. Allow to evaporate spontaneously, or if

[1] In cases of powder mixtures or tablets containing ground celery seed, much coloring matter, cinchona alkaloids, laxative or extractive principles other than acetanilid or phenacetin, it is our practice to shake out the latter by means of chloroform from dilute sulphuric acid solution.

[2] In case the preparation contains ground celery seed or certain oily principles, it sometimes happens that the acid solution does not become entirely clear at this point.

desired on a steam or hot-water bath to dryness, in the latter case partially covering the dish toward the end of operation with a watch-glass in order to avoid possible loss from "popping." Cool in desiccator and weigh as caffein, dry alkaloid.[3]

Acetanilid.

First Method.—The acid solution remaining in the separator and containing aniline sulphate is run into a 100 c.c. Erlenmeyer, the filter through which the chloroform passed is washed once with a little water, allowing the latter to run into the separator. Rinse the latter thoroughly, adding the aqueous rinsings to the acid solution. Now, run in slowly and with constant agitation a standard solution of potassium bromide-bromate [4] to a faint but distinct yellow coloration. The number of cubic centimetres employed, multiplied by the value of 1 c.c. in terms of acetanilid, will give the amount of acetanilid present.

Second Method.—The acid solution aforesaid is treated with successive small portions of sodium bicarbonate until an excess of this reagent is observed in the bottom of the separator. Add 50 c.c. of chloroform and 15 to 20 drops of acetic anhydride, shake for some time vigorously, allow the chloroform to clear, then pass through the same filter used for the caffein into a 100 c.c. Erlenmeyer, and distil off most of the chloroform. Use this distillate for a second shake out, clear, filter, and distil down to a small volume, transferring the residue and the subsequent chloroform

[3] Should the caffein not be colorless or nearly so, the residue is dissolved in about 10 c.c. of water, filtered, if necessary (in case oily matters are present), through a wet filter, the filtrate acidified with dilute hydrochloric acid, the caffein precipitated with 15 to 20 c.c. of Wagner's reagent, allowed to stand a half hour, filtered, and the precipitate washed with a few cubic centimetres of same reagent, the filter, together with precipitate, transferred to separator, decolorized by means of sodium sulphite, and the caffein finally extracted with chloroform.

[4] For this purpose the solution is prepared by adding bromin in slight excess to a concentrated aqueous solution of 50 grammes caustic potash, the liquid diluted till the separated salts redissolve, boiled, to expel any excess of bromin, and finally made up to 1 litre. This solution is standardized with weighed amounts of acetanilid, or it may be so adjusted by further dilution that 1 c.c. is exactly equivalent to 1 centigramme of acetanilid. For purposes of titration 1 to 2 decigrammes are heated a half hour on the steam or water bath with 10 c.c. of dilute sulphuric acid.

washings to a tared beaker or dish precisely as in the case of caffein. Allow the solvent to evaporate spontaneously or by means of a blast

RESULTS OBTAINED IN THE CO-OPERATIVE WORK ON AN ACETANILID MIXTURE.

Analyst.	Caffein	Acetanilid.		Soda bicarbonate.		Total.[6]
		Volumetric.	Gravimetric.	Volumetric.	Gravimetric.	
	P. ct.	*P. ct.*	*P. ct.*	*P. ct.*	*P. ct.*	*P. ct.*
L. A. Brown, North Dakota	12.16	65.93	.....	23.20	.....	101.29
	10.93	66.10	.....	.....	23.50	100.53
	11.05	65.93	.....	.....	23.20	100.18
	10.40	66.10	.....	.....	.....	.....
L. D. Havenhill, Kansas	11.50	63.00	.....	.....	25.10	99.60
	10.73	61.50	.....	.....	25.00	97.23
	11.33	63.40	.....	.....	24.90	99.63
	11.53	63.44	.....	.....	25.00	99.97
H. L. Schulz, Michigan	11.00	63.00	.....	.....	24.60	98.60
	11.00	62.00	.....	.....	24.80	97.80
H. A. Seil, New York	10.55	65.78	.....	.....	25.03	101.36
	10.49	.....	65.26	.....	25.11	100.86
T. F. Darling, New York	10.48	65.80	.....	.....	25.13	101.41
	10.62	.....	67.72	.....	25.13	103.47
E. L. Redfern, Nebraska	9.80	65.10	.....	.....	25.06	99.96
	10.06	64.58	.....	.....	24.93	99.57
	9.93	63.03	63.60	.....	25.00	98.25
	10.20	63.21	63.80	.....	24.93	98.64
E. M. Bailey,[5] Connecticut	10.90	64.53	.....	.....	25.07	100.50
	11.17	64.00	.....	.....	24.54	99.71
C. B. Morrison,[5] Connecticut	11.30	.....	.....	25.93	25.57	.....
	11.37	.....	.....	25.67	25.33	.....
	10.67	64.80	.....	25.93	25.43	101.15
A. R. Mehrtens, California	10.30	64.53	.....	.....	24.99	99.82
G. E. Colby, California	10.00	65.33	.....	.....	24.79	100.12
W. O. Emery, Washington, D. C.	10.23	64.79	.....	.....	24.92	99.94
	10.29	64.85	.....	.....	24.95	100.09
	10.01	.....	64.68	.....	25.01	99.70
Average	10.71	64.38	65.01	25.18	24.89	99.98
Maximum	12.16	66.10	67.72	25.93	25.57	103.47
Minimum	9.80	61.50	63.60	23.20	23.20	97.23
Difference	2.36	4.60	4.12	2.73	2.37	6.24
Known composition of acetanilid mixture (acetanilid, 453 parts; caffein (anhyd.), 70 parts; soda bicarbonate, 174 parts)	10.04	64.99		24.96		99.99

[5] Reported by J. P. Street.

[6] In cases where two percentages for volumetric and gravimetric determinations of the same substance were reported, the mean of such percentages has been taken in computing the total percentage.

or fan, avoiding, however, undue heat.[7] Dry in desiccator over quicklime to constant weight.

Verify the final weight by means of titration with standard potassium bromide-bromate solution as in the first method. Heat the residue with 10 c.c. dilute sulphuric acid a half hour on the steam or vapor bath, cool, add 5 c.c. of water, and titrate as directed above.

Sodium Bicarbonate.

The residue left after the first treatment with chloroform is weighed when dry and represents very nearly the amount of sodium bicarbonate present. It may be more accurately estimated by titrating with tenth-normal sulphuric acid, using congo red as indicator, or it may be ignited with dilute sulphuric acid and weighed as sodium sulphate.

Calculate results in parts per 100.

The results reported are tabulated as follows:

Owing to an ambiguity in the expression "dilute sulphuric acid" employed in the method under caffein, as also in the footnote, page 482, for standard bromide-bromate solution, some of the workers quite naturally used the Pharmacopœial strength, with the result that the acetanilid was not completely hydrolyzed. This undoubtedly explains the somewhat high results for caffein and the correspondingly low ones for acetanilid. The strength of acid intended and the one actually employed for this purpose in the Bureau of Chemistry is that ordinarily used in laboratory work and is made by diluting 1 part of concentrated sulphuric acid (whose specific gravity is not less than 1.826 at 25°) with 5 parts of water. From two to three hours' heating on the steam bath is usually required to completely hydrolyze the acetanilid.

Notwithstanding this ambiguity the results obtained are very gratifying, in view of the fact that the method is new and the workers have entered into a comparatively new field. The percentages of variation are so small as to almost warrant the referee in recommending it as a provisional method to the association. He believes, however, that the method should receive additional study, and so recommends. It is also recommended that additional mixtures be tested with this and such other methods as may be found desirable.

[7] Acetanilid suffers appreciable loss when heated above 40°.

THE FORTY-SIXTH ANNUAL MEETING OF THE BRITISH PHARMACEUTICAL CONFERENCE.

By John K. Thum, Ph.G.

Apothecary at the German Hospital, Philadelphia.

The British Pharmaceutical Conference held its forty-sixth annual meeting at Newcastle-on-Tyne, July 26–29 of this year.

The following review was obtained from the reports published in the British pharmaceutical journals.

As usual the Conference commenced its proceedings with the President's reception. This social function took place in the buildings of Armstrong College, Barras Bridge. The Lord Mayor cordially welcomed the Conference to the city. Professor Lebour, Vice-Principal, on behalf of the College authorities welcomed the delegates and mentioned how well pleased he was with the scientific aims of the Conference. Mr. J. F. Tocher, the President, thanked the speakers for their kind welcome.

The visitors then passed into the physical and electrical laboratories and were shown a number of interesting experiments by Professors Stroud and Thornton. Wireless telegraphy, X-rays, high-tension electrical experiments, optical experiments, the singing arc, melting iron under water, the jumping coil, floating iron-bar, and oxy-acetylene welding were a few of the interesting experiments shown. There was also an excellent exhibit of a technical nature of things interesting to progressive pharmacists.

On Tuesday morning the regular sessions opened with the President in the chair.

Mr. Weddell, on behalf of the local committee, delivered a speech of welcome. The President replied by thanking Mr. Weddell and his colleagues for the arrangements they had made for the comfort of the Conference. After the reading of several letters of regret, prominent among them being one from the veteran founder Dr. John Attfield, the President read his address.

"Some Problems of Interest to Pharmacists To-day" was the title of Mr. Tocher's address. He called attention to the fact that Newcastle was the scene of the Conference's birth. The institution of it as an organization for the encouragement of pharmaceutical research was an event of the greatest importance to British phar-

macy. The extent to which scientific pharmacy has been enriched by the results of work done by the Conference cannot at the present time be accurately estimated. He says that the reasons for the existence of the organization are a "consistent desire as a body to develop pharmacy, to maintain past traditions, to ensure proper training for future entrants, to extend research, all for the one purpose, namely, of securing for the public the proper administration of medicinal compounds, while at the same time acting as guardians of the public weal with respect to poisonous materials of all kinds."

In speaking of patent medicines he says that from the medical standpoint they are of doubtful service to the community. The imposition of a heavier stamp duty than the one now in force should be imposed on articles held out to have curative properties.

Discussing pharmacopœial revision, he gives it as his opinion that it should be the duty of the committee not only to conduct experiments but at the same time to make an organized attempt to glean the experience of pharmacists generally, and invite men outside the committee to undertake definite sections of work, repeating what may have been done by the committee. He said it is because of the embodied results of a few experiments of one person that inadequate formulæ have appeared in the Pharmacopœia. He also makes the assertion that there is no publication in the whole Kingdom better fitted for a scheme of co-operative investigation than is the British Pharmacopœia. Mr. Tocher concluded his remarks by calling attention to the rapid development of chemical science in every direction and the profound effect it is having on the theory and practice of pharmacy.

Taking it altogether, Mr. Tocher's address was a most excellent exposition of pharmaceutical problems confronting the British pharmacist of to-day and certainly is worthy a careful reading by American pharmacists, particularly that portion which relates to pharmacopœial revision.

After the reading of the annual report, the reading of the financial statement, and the transaction of other routine business, the President called for the reading of papers, abstracts of which follow.

Experiences in the Testing of Drugs by Biochemical Methods, with Special Reference to Digitalis, Squill, and Strophanthus.

By William Martin.

The author gives the result of his work in testing biochemically, various drugs, such as cannabis indica, ergot, epinephrin, and the cardiac drugs mentioned in the title of his paper. He agrees with Professor Marshall that the main cause of deterioration of extract of cannabis indica is oxidation of the active constituent, and that storing in tightly sealed vessels would tend to secure greater uniformity. He agrees that generally good results are obtained from fluidextract of ergot, although the differences in activity are sufficient proof that much improvement could be made in the official preparations of ergot.

His method for testing the cardiac tonics is one which requires a fatal termination to follow the giving to a frog of a fixed dose of the preparation tested within a certain time-limit. That considerable variation exists in the physiological action of preparations of these cardiac drugs, particularly digitalis, is the conclusion at which he arrives. Dr. Martin thinks that biochemical testing could and should be undertaken by pharmacists.

Estimation of Extractive and Glycerin in Spirituous Galenicals.

By W. A. H. Naylor and E. J. Chappel.

The authors' method consists of distilling, under reduced pressure and in a current of steam, a sample of the preparation to be tested. The distilled portion is evaporated to a definite volume and an aliquot part used for determining glycerin by the use of Hehner's bichromate method as modified by Richardson and Jaffé, the treating with lead subacetate being omitted. The extractive which remains in the flask is dried at 110° C., and weighed.

The Constituents of the Rhizome of Cimicifuga Racemosa.

By Horace Finnemore.

Water, light petroleum ether, chloroform, ethyl acetate, and alcohol were used in the treatment of an alcoholic extract of the rhizome. The aqueous contained a small quantity of isoferulic

(hesperetic) acid, 3-hydroxy-4-methoxy cinnamic acid (m.p. 228° C.). Sugar, tannin, and a crystalline substance (m.p. 153° C.) were also found. The petroleum-ether treatment yielded phytosterol, palmitic acid, and liquid fatty acids containing oleic and other unsaturated acids. Treatment with the ethereal solution gave a colorless crystalline substance; and two crystalline substances were isolated from the chloroformic solution. A trace of an alkaloidal body was discovered. The specimen of "racemosin" in the museum of the Pharmaceutical Society has been examined and found to correspond with the chloroformic extract obtained by the author.

Commercial Emulsions.

By E. W. Pollard.

The author spoke of the different methods of analysis and gave the results of working with a method of his own for the assay of the percentage of oil in samples of emulsion. He defines a good emulsion as being no more viscous than glycerin, it should throw down no precipitate on being diluted, and the oil globules should not exceed 15 μ.

Should the Dispensing of Medical Prescriptions be Exclusively Confined to Pharmacists?

By James Fowler Tocher.

According to the author the great grievance which the pharmacists of England have above all others is the fact that while they are specially educated and trained to do so, most of the dispensing of prescriptions is done by the medical profession. He says that it must be recognized that it has been the practice for many years for doctors to supply their own physic, yet, as they have no practical training to speak of in pharmacy, he must answer the above question in the affirmative. The absolute transference of the dispensing of medicine from medical men to pharmacists would, in his opinion, be accompanied with advantages to the doctor, the pharmacist, and the public, although in remote rural districts it would be advantageous to the patient for the physician to dispense the remedies required. The dispensing practitioner, he says, is both a trader and a professional man. He ceases to be a trader the moment he stops selling medicine. The origin, properties, preparation, and dispens-

ing are the pharmacist's special sphere. The advantages to the public are many. Without necessarily implying inaccuracies in dispensing by medical men, or doubting their skill in the mixing of medicines, dispensing by pharmacists is advantageous to the public because their compounding to the medical man's prescribing is of the nature of a check on both.

Problems of the Poison Schedule.

By H. Wippell Gadd.

The author, after a few introductory remarks, proceeded to comment upon some items in the Schedule, contrasting the 1868 and 1908 entries, commenting especially on the latter.

Antimonium Sulphuratum.

By F. H. Alcock.

After speaking of its rather scant use in medicine, the author devoted considerable time to its important use in the manufacture of rubber. He states that it is liable to contain harmful impurities, generally thiosulphate.

Determination of Antimony in Sulphide Preparations.

By David Lloyd Howard and J. Bristowe P. Harrison.

The authors give an assay for antimony sulphides which can be worked more rapidly and with less trouble than the gravimetric process. It consists, practically, in fusing the sulphide with sodium hydroxide, which converts the antimony into sodium metantimonate, which, when brought into solution and reduced to the lower state of oxidation, is determined volumetrically by means of standard iodine solution. The sulphur, which is oxidized to sulphuric acid, is determined by precipitation as barium sulphate.

Concerning the Quantitative Determination of Free Salicylic Acid in Bismuth Salicylate.

By J. Bristowe P. Harrison.

The result of extraction of the free acid by the use of ether, petroleum-ether, acetic-ether, acetone, chloroform, and benzol (90

per cent.) showed that ether and chloroform are the most suitable solvents to use.

Unguentum Paraffini.

By J. H. Franklin.

The author, after experimenting with paraffin wax of different melting points, white beeswax, commercial bleached ceresin, pure bleached ceresin, commercial bleached carnauba wax, and pure yellow carnauba wax, comes to the conclusion that a mixture of white petroleum jelly, 85 parts, and pure bleached ceresin, 15 parts, makes a firmer, smoother, and more homogeneous ointment than that now official.

Fluidextract of Cascara Sagrada.

By Charles Symes.

The author obtained a more active preparation by the process outlined below.

The B.P. directs that the bark be macerated six hours with distilled water, then percolated with the same menstruum until exhausted, the percolate evaporated and made up to a given volume with dilute alcohol; the freedom from bitterness determining complete exhaustion.

In preparing some fluidextract, when bitterness had ceased, the author continued the percolation with some ammonia added to the menstruum, and upon subsequent evaporation obtained a yield of extract possessing medicinal properties; this was added to the first evaporated portion and diluted alcohol added to required volume. The same result was obtained on repeating the process at a subsequent date. He recommends this method as tending to more completely exhaust the cascara.

Cacao Butters and Cacao-butter Substitutes.

By W. B. Cowie and B. M. Brander.

The authors give the results of an examination of two substitutes of cacao butter, one so well prepared that it responded to most of the tests for genuine cacao butter. These substitutes were compared with the genuine and one made from cacao husk.

Björlund's ether test was used as a preliminary, and the results were as follows:

	Cooled to 0° C. for 3 minutes.	Clear at 0° C.
1. Genuine cacao butter	no deposit	15
2. Husk cacao butter	no deposit	14
3. Hard cacao-butter substitute	flaky deposit	15
4. Soft cacao-butter substitute	slight deposit	21 (still cloudy)

Further determinations were carried out.

Refractometric Examinations of Galenical Preparations.

By W. B. Cowie and T. O. Broadbent.

The authors give a method for detecting adulterations in galenicals by the determination of the refractive index. They claim that the refractive index agrees with the specific gravity and amount of extractive.

A Preliminary Examination of Euphorbia Pilulifera.

By J. Stableford Hill.

The investigation of this drug by the author seems to show the presence of an alkaloid, tannic acid, a waxy substance, several resins, and no volatile oil.

His method for determining the presence of an alkaloid was as follows: The finely powdered drug was exhausted with Prollins's fluid, and the solution, after concentrating, treated with very dilute sulphuric acid; it was then filtered, washed in ether, made alkaline with sodium hydroxide, and shaken out with a mixture of ether (3 parts) and chloroform (1 part). The residue was dissolved in 20 c.c. of 0.2 per cent. sulphuric acid solution and tested with the usual alkaloidal reagents. Thresh's and Mayer's reagents threw down characteristic precipitates.

Note on the Separation of Strychnine from Brucine.

By G. Pinchbeck.

The author gives a tabulation of the results obtained by various workers who used the U.S.P. process, including work done by himself with the same process. He then gives a modification of the

U.S.P. process, which he asserts is capable of giving accurate results, and when compared with the technic required and the time consumed in using the ferrocyanide method or Gordon and Prescott's periodate, is certainly not tedious to the worker.

The Use of Alcohol in Pharmacy.

By D. B. Dott.

A number of pharmaceutical preparations are mentioned of which the author thinks the alcoholic content can be reduced without any consequent diminution of the therapeutic activity. He also suggests the use of glycerin for many drugs in place of alcohol as a solvent and preservative; he also refers to the work of Squibb and others in exhausting drugs with dilute acetic acid as a solvent. The recommendation by the author that methylated spirit should be authorized in preparations of liniment we deem rather unwise.

p-Hydroxyphenylethylamine, an Active Principle of Ergot, Soluble in Water.

By G. Barger.

The author summarizes recent work on a new active principle of ergot. Barger and Dale pointed out that the alkaloid ergotoxine, while being responsible for many of the characteristic effects of ergot, is only present in very small quantities in most specimens of preparations of it; such of these specimens as possess any appreciable activity were therefore regarded as having a second active principle. The physiological properties of p-hydroxyphenylethylamine, recently isolated from putrid meat by Barger and Walpole, suggested that this base might be the above-mentioned active principle of aqueous extracts of ergot. The author states that it has been possible to prove that this active principle occurs in such an extract, and its presence accounts for such of the activity as is not due to small quantities of ergotine.

The method of isolation has recently been described in detail by Barger.

Malt Extract with Cod-liver Oil.

By E. F. Harrison.

The author gives a tabulated result of his investigation of various specimens of malt extract with cod-liver oil found on the

market. He also gives in detail his method for determining the amount of oil present and the diastatic value of the extract.

The Comparative Examination of the Halogen Absorption of Oils by the Methods of Hubl, Wijs, Hanus, and McIlheney.

By J. S. Remington and H. Lancaster.

In determining the halogen absorption of linseed, lard, and rape oil, by the above methods, the authors arrive at some interesting conclusions. They find that better results can be obtained by the Wijs than by the Hubl or Hanus methods. More concordant results are obtained in the dark than in the light with the Wijs and Hanus methods. They also state that the bromine process of McIlheney is practically instantaneous, and because of its rapidity and inexpensiveness is preferable to any of the iodine methods.

This concluded the reading of papers. Mr. Peck, on behalf of the Cambridge Pharmaceutical Association, invited the Conference to meet next year at Cambridge. The invitation was accepted. Election of officers was then proceeded with and resulted as follows: President, F. Ransom, Ph.C., F.C.S. (Hitchin); Hon. Treasurer, J. C. Ummey (London); Hon. General Secretaries, E. S. Peck (Cambridge) and H. Finnemore (London).

NEW ESSENTIAL OILS.*

Oil from Barosma Pulchellum.—In addition to the varieties of Barosma which are of interest in the preparation of buchu leaf oil, *i.e., Barosma betulinum* (Thumb.) Bartl. et Wendl., *B. crenulatum* (L.) Hook., and *B. serratifolium* (Curt.) Willd., the leaves of other species have lately been met with in the London market on several occasions. Some years ago, Sage[1] reported on leaves of *Diosma succulentum* var. *Bergianum,* known as Karoo Buchu, which are reputed to yield an oil equalling that of *Barosma betulinum* in

* From the Semi-Annual Report of Schimmel & Co., April, 1909.

[1] *Chemist and Druggist,* 65 (1904), 506, 717. Report April, 1905, 12.

value. In other quarters, however, leaves have also been noticed of which the oil, by its mere odor, betrays a composition differing materially from that of the ordinary buchu leaf oil. The leaves of *Barosma pulchellum* (L.) Bartl. et Wendl., as well as those probably derived from *Agathosma variabile* (Lond.) belong to the latter category. The last-named leaves have also been described by Sage[2] who, on account of their anise-like odor, called them "Aniseed Buchu." These leaves are ovate-lanceolate, leathery, 5 to 8 mm. long and 3 mm. wide, and bear a resemblance to Karoo Buchu. Sage intends to make further investigations with the object of discovering whether the botanical designation aforementioned is correct.

E. M. Holmes[3] was the first to call attention to the occurrence of leaves from *Barosma pulchellum*. They differ from the *betulinum* leaves by their citronella-like odor as well as by being smaller. Their length runs from 7 to 12 mm., their width is 4 mm. They have very short stalks, are ovate to ovate-lanceolate, serrulate, obtuse, and broadest at the base of the leaf. Like the other varieties of *Barosma*, the shrub is a native of Cape Colony. In order to enquire further into the question whether the oil would eventually possess a commercial value, we obtained from London a considerable parcel of the leaves. Dr. Giessler, "Custos" at the Botanical Institute of Leipzig University, who has examined the material as regards its botanical origin, has ascertained that it really represented *Barosma pulchellum* (L.) Bartl. et Wendl. Leaves of the closely related *B. pulchellum* var. *majus* and *B. latifolium* (L. f.) Röm. et Schult. also occurred in the parcel.

Upon distillation the leaves yielded 3 per cent. of a golden-yellow oil, with an odor reminding chiefly of citronella, but possessing at the same time an unpleasant narcotic subsidiary odor, which constitutes a direct objection to the use of the oil. The specific gravity was 0.8830 (15°), opt. rot. $\alpha_D + 8° 36'$, $n_{D20°}$ 1.45771, acid no. 18.5, ester no. 27.2, ester no. after acetylation 237.0 = 79.3 per cent. $C_{10}H_{18}O$. We are able to give the following details with regard to the examination of the oil, which is, however, not yet concluded:

The disagreeable subsidiary odor referred to above is due to a base. This was abstracted from the oil (which was kept cool) by treatment with 25 per cent. tartaric acid solution. The base, sepa-

[2] *Pharmaceutical Journal*, 80 (1908), 125.

[3] *Pharmaceutical Journal*, 79 (1907), 598; compare also *Chemist and Druggist*, 71 (1907), 702.

rated from the tartaric acid solution by means of carbonate of soda, possessed an extraordinarily penetrating narcotic odor. It had a rather inconstant b. p. between 130° and 140° (5 mm. press.). (The quantity of the material employed was barely 1 Gm.) From the hydrochloric acid solution, on treatment with platinum chloride, no crystals separated off.

The citronella-like odor of the oil freed from the base made us suspect the presence of citronellal. As a matter of fact the oil reacted with bisulphite liquor partly neutralized by sodium carbonate, a crystalline mass being separated. From the latter, after filtering with the suction pump and purifying with alcohol and ether, an aldehyde was liberated by warming with carbonate of soda solution. Its constants showed it to be citronellal; b. p. 73° to 75° (7 to 8 mm. press.), b. p. 205° to 208° (atmosph. press.), $d_{21°}$ 0.8560, α_D + 13°6′, $n_{D20°}$ 1.44710. Its semicarbazone melted at 81° to 82°. From 500 Gm. of oil we isolated about 220 Gm. of aldehyde. The smaller part of the oil freed from citronellal passed over between 45° and 103° (5 mm. press.), the larger portion remained behind in the flask in the form of a brown, viscous oil. The fractions with the lowest b. p. contained small quantities of methylheptenone, which was separated in the form of a semicarbazone. Only after recrystallizing it three or four times from dilute alcohol the m. p. of this derivative was found to be 134° to 135°. This circumstance, as well as the fact that when the odor observed was not that characteristic of methylheptenone, but rather reminded of a saturated fatty ketone, indicated the presence of another, additional, ketone. The semicarbazone referred to above, when mixed with that from the pure methylheptenone, showed no depression of the melting point.

In a fraction having the b. p. 75° to 82° (5 mm. press.) and the opt. rot. + 6° 54′, small quantities of d-menthone could be detected, but only through the semicarbazone. Only when the oil mixed with it had been removed from the semicarbazone solution by steam distillation, the derivative could be obtained in the solid form. After repeated recrystallization from alcohol it melted at 178° to 181°, and when warmed with diluted acid it developed the unmistakable odor of menthone. Efforts were also made, unfortunately without success, to separate by means of the oxime larger quantities of menthone from the fractions which preceded and succeeded the one referred to above, and to reconstitute the ketone from them. It is therefore probable that the somewhat pronounced odor of mint

which attached to all these fractions is ascribable to the presence of isopulegol. This isopulegol obviously owed its existence to the action of acids upon the citronellal.

Further, in the portions of the oil boiling between 75° and 103° (5 mm. press.) we discovered an alcohol of a rose-like odor, which was ascertained to be d-citronellol. For the purpose of identification the fractions were treated in the well-known manner with phthalic anhydride. The citronellol, separated by saponification from the solution of the sodium salt of the acid phthalic ester and distilled over with water vapor, possessed the following constants: b. p. 93° to 95° (5 to 6 mm. press.), $d_{15°}$ 0.8732, α_D + 2° 14′, $n_{D20°}$ 1.46288. The silver salt prepared from the free acid phthalate, after being recrystallized from benzene and methyl alcohol, showed the characteristic melting point for this salt (125°) and the theoretically required silver content:

0.2774 g. sbst.: 0.0727 g. Ag.

Found:	Calc. for $C_{18}H_{21}AgO_4$:
Ag 26.21 per cent.	26.23 per cent.

When the original oil was treated with highly-diluted soda liquor it proved to contain an oily acid of a high b. p. as well as traces of a phenol. In order to separate these two the oil, after being recovered from the soda liquor, was treated with carbonate of soda solution. The acid which had separated from the carbonate solution on acidulation may, however, not be a uniform one, as might be concluded from its b. p. and its behavior as detailed below. Apart from an unimportant first runnings (b. p. 115° to 125°, 5–6 mm. press.) it boiled at 125° to 131°. Its other constants were as follows: b. p. 257° to 263° at normal press., $d_{15°}$ 0.9394, α_D + 5° 2′, $n_{D20°}$ 1.45611. These properties, and the silver content as ascertained by analysis of its silver salt recrystallized from water, indicate citronellic acid $C_{10}H_{18}O_2$:

0.3079 sbst.: 0.1196 g. Ag.

Found:	Calc. for $C_{10}H_{17}AgO_2$:
Ag 38.84 per cent.	38.77 per cent.

In order to identify the acid more closely recourse was had to the amide of citronellic acid, m. p. 81° to 82°. For its preparation, the acid was first converted into the chloride (b. p. 122° to 125°, 6 mm.)

by means of thionyl chloride, and the latter converted into the amide with aqueous ammonia. The amide purified from petroleum ether melted not quite sharply at 87° to 88°, that is to say, 6° higher than that obtained by Tiemann[4] from citronellic acid nitrile. It is our intention, for purposes of comparison, to prepare the amide of synthetic citronellic acid, in order to determine by this means whether the above-mentioned acid really represents citronellic acid (the existence of which in essential oils has not been detected up to the present), or another acid of the same constitution. In addition to the arguments adduced above, its identity with citronellic acid seems to be indicated by the fact that the oil contains both citronellol and citronellal.

Only traces of the phenol referred to above were at our disposal. These were just sufficient to enable us to identify it by its benzoyl combination. This body, obtained by Schotten-Baumann's method, when purified from petroleum ether, had a m. p. of 109° to 110°, but up to the present we have been unable to identify it with the benzoate of any known phenol.

From the Instituto Médico Nacional in Mexico we received the two following distillates:

Oil of Satureja macrostema (Benth.) Briq. (*Calamintha macrostema* Benth.).—The oil of this shrub-like plant, which belongs to the N. O. *Labiatæ* and is a native of Mexico, was pale yellow and had an odor resembling that of mint; $d_{15°}$ 0.9182, $\alpha_D + 6° 51'$, $n_{D20°}$ 1.46852, acid no. 15.6, ester no. 10.3, ester no. after acetylation 37.9. The oil is soluble in any proportion of 90 per cent. alcohol, also in 3 vols. of 70 per cent. or 1.2 vol. of 80 per cent. alcohol, but opalescence ensues with the last two when more of the solvent is added. The odor points to the presence of pulegone.

Oil from the Mexican Marsh-cypress (*Taxodium mexicanum* Carr., *T. Montezumæ* Decne., *T. mucronatum* Ten.).—This tree, which belongs to the conifers and is known in Mexico as "Sabino," grows in that country at altitudes of from 5600 to 7000 ft. It is not distributed over a very wide area, but where it does grow it forms large forests.[5] The oil, which had probably been distilled

[4] *Berl. Berichte*, 31 (1898), 2899.

[5] The famous "Cypress of Montezuma" in the cemetery of Santa Maria del Tule near Oaxaca belongs to the same variety. It is said to be 130 ft. high, the trunk to have a circumference of 98 ft. De Candolle estimated its age at 6000 years, Humboldt at 4000.

from the leaves, was of a pale brown color and somewhat resembled in its odor, oil of turpentine, to which it is probably also closely allied in its composition. $d_{15°}$ 0.8685, a_D — 10° 20′, $n_{D20°}$ 1.46931, acid no. 0.5, ester no. 5.7; soluble in 5.4 vols. and more of 90 per cent. alcohol.

Oil of Artemisia Herba-alba var. densiflora Bois (Chieh Oil).—From Egypt we received, for the purpose of examining it for essential oil, an herb which is known there by the name of "Chieh," and which occurs on the high limestone plateaus of Egypt and Tripoli and probably also in Arabia. The plant is said to reach its full development early in March and to flourish particularly in rainy years. The Arabs and Tuaregs employ a decoction of the herb medicinally as an emollient and diuretic. Owing to the sample sent to us being imperfect, great difficulty was experienced in determining its botanical name. Prof. Heckel, of Marseilles, who kindly examined the sample for us, and to whom we owe thanks for his courteous assistance, informed us under reserve that the herb was probably an *Artemisia Herba-alba.* This opinion was confirmed on further investigation when a few specimens which had been carefully pressed between paper were sent to us. Dr. Giessler, "Custos" at the Botanical Institute of the University of Leipzig, was able to ascertain that the sample represented a variety of the above-mentioned plant, viz., *A. Herba-alba* var *densiflora* Bois.

By water vapor we obtained from it a yield of .16 per cent. of a yellowish oil, with a clear odor of thujone, which upon examination gave the following results: $d_{15°}$ 0.9192, a_D — 5° 20′, $n_{D20°}$ 1.45611, acid no. 1.5, ester no. 11.0, ester no. after acetylation 40.7, soluble in 2.6 vol. and more of 70 per cent. alcohol. From the low ester and acetylation numbers it is to be inferred that the oil contains but small proportions of saponifiable and alcoholic constituents.

With regard to an oil of *Artemisia Herba-alba* previously examined by E. Grimal, compare our Report October, 1904, 13. This oil differs entirely from the one now under review, which may without further inquiry be set down to the fact that *A. Herba-alba* shows very wide variations. Several varieties exist which have been regarded as separate species by many authors; J. Gay, for instance, describes the variety above-mentioned as *A. Oliveriana.*

AMPULS.*

Ampuls, or "Einschmelz gläser" as Hager calls them in his "Handbuch der Pharmazeutischen Praxis," are no new thing. Twenty-two years ago Limousin, a French pharmacist, published a paper in the *Bulletin générale de Therapeutique,* describing what he called "ampoules hypodermatique" for preserving hypodermic solutions in a sterile condition.

The use of these ampuls did not appear to appeal to the medical profession until within recent years, and then only to physicians of France and those of South America. The Swiss Pharmacopœia in the chapter on sterilization gives some information as to their preparation.

There are quite a variety of forms of ampuls. That of Limousin's was a spherical bulb with a capacity of 1–2 c.c., with a fine drawn neck about an inch and a quarter long. The most practical form of ampul is that with a wide flat bottom; such a one enables the physician to fill his syringe without the necessity of a second person holding the ampul for him. Some have the shape of an ordinary chemical flask, while many are merely pieces of glass tubing with the ends somewhat drawn out and sealed. It seems that with this last form there is less danger of breakage in the final sterilization of the filled ampul. It is highly important that the ampul be made of neutral glass. Any glass with soluble alkali in its composition will in time precipitate alkaloids present in hypodermic solutions. An absolutely non-alkaline glass is made in Germany called Jena Normal, 16iii, and ampuls made from this glass are now obtainable.

Too much stress cannot be laid on the importance of complete sterilization whenever practicable. Some alkaloidal solutions may be subjected to a heat of 100° C. without decomposition, while others will decompose at that temperature and can only be sterilized by heating to 50° or 60° C. at repeated intervals for several days. Hager mentions atropine, cocaine, hyoscine, scopolamine, duboisine, physostigmine, atoxyl, and ergot solutions as substances that will not stand heating to the boiling point of water.

Whether the filled ampuls always receive a final sterilization or not there should always be great care exercised in preliminary sterilization. That is to say, the empty ampuls, whether bought

* Abstract of C. A. Mayo's paper on "Ampuls and Their Use in the Dispensing of Hypodermic Solutions," in *American Druggist,* vol. liii, p. 379.

or made by the pharmacist, should be "placed in a beaker filled two inches deep with water, the water brought to a quick boil, removed from the heat, and cold water poured in. This process creates a vacuum in the ampul which is filled by water drawn up into the bulb." The water is then boiled, which process expels it from the ampul; the ampul is taken out and dried over a flame and kept under aseptic conditions until filled. In the meantime the hypodermic solution that is to be used should be prepared and sterilized. The character of the alkaloid used will determine the degree of temperature it will stand in sterilization.

There are a half dozen ways of filling ampuls: (1) by means of a graduated pipette; (2) a burette; (3) a hypodermic syringe; (4) a vacuum made by heating the bulb; (5) a vacuum obtained by the use of ether.

In the case of the methods just mentioned it is absolutely essential that the filled ampuls be subjected to a final sterilization. "In the next process, by aspiration with the aid of an Auer apparatus, which, from a bacteriological point, is much to be preferred, there is fair assurance that when properly carried out the bulbs will be entirely sterile when filled, but even in this case it might be desirable to sterilize the sealed bulbs after the lapse of twenty-four hours." Too much emphasis cannot be placed on the care and attention the operator should give in obtaining complete sterility in the finished ampul. Filled ampuls should be boiled or sterilized in a steam sterilizer for half an hour for two days.

While it is doubtful whether ampuls will become popular in this country, on account of cost in labor involved, yet it is right and proper that the retail pharmacist know how to prepare them if requested by his neighboring physicians.

JOHN K. THUM.

BOOK REVIEWS.

A TEXT-BOOK OF PHYSIOLOGICAL CHEMISTRY for students of medicine. By John H. Long, of the Northwestern University Medical School. Second Edition, revised, with 42 illustrations. Philadelphia: P. Blakiston's Son & Co. $2.50 net.

In this work Professor Long, who is well known for his researches and wide experience in matters of public health, has pre-

sented in an unusually clear and readable manner the fundamental facts and theories of physiological chemistry. The following subjects are considered: (1) the nutrients and related substances; (2) ferments and digestive processes; (3) the chemistry of the tissues and secretions of the body; (4) the end products of metabolism, including excretions and energy balance.

In this revision a number of important changes have been made. In a number of chapters, notably in the consideration of proteins,—the newer work has been included. "A much fuller discussion has been given to the subject of the urine, and a new chapter has been added on the methods of urine analysis. These methods embrace not only the usual clinical tests, but the most important quantitative processes, in certain directions, as well, and are given in sufficient detail for practical metabolism work."

Many experiments are included in the book, and while it is primarily intended for the use of scientific schools, where preparation for a medical course is given, and for chemical courses in medical schools, it would prove a very valuable book for postgraduate work in pharmaceutical colleges and schools.

ESSENTIALS OF BACTERIOLOGY. By M. V. Ball, M.D. Sixth Edition, thoroughly revised, with 135 illustrations, some in colors. Philadelphia and London: W. B. Saunders Company, 1908. $1.00 net.

This is a good compilation and will be very useful in connection with a laboratory course in bacteriology. In the first part a general consideration of bacteriology is given, together with a fairly good treatment of the technic involved. In Part II are considered: non-pathogenic bacteria; pathogenic bacteria; pathogenic bacteria for animals but not for man; yeasts and moulds; the examination of air, soil, and water; bacteriologic examination of the organs and cavities of the human body; and finally antiseptics and antisepsis.

ARBEITEN AUS DEM PHARMAZEUTISCHEN INSTITUT DER UNIVERSITÄT BERLIN. Herausgegeben von Dr. H. Thoms. Sechster Band. Mit 4 Abbildungen. Berlin and Wien: Urban & Schwarzenberg, 1909.

The present volume contains the work done at the Pharmaceutical Institute of the University of Berlin during the year 1908. There are some eighty-six papers dealing with the examination of

new preparations and patent medicines; researches in organic chemistry, the examination of food products, new studies on the technical and other products from the Colonies, new apparatus, and several interesting essays by Dr. Thoms.

It is fortunate that very many of these papers have been published in the *Apotheker-Zeitung*, the organ of the German Apothecaries' Society, as they should be more widely read and accessible than are the separate publications of the Institute. Some of these articles will be abstracted for this JOURNAL later.

HANDBUCH DER PHARMAKOGNOSIE von Dr. A. Tschirch. Leipzig: Chr. Herm. Tauchnitz. Vollständig in circa 30 Lieferungen zum Preise von je 2 Mark.

Up until the present time twelve brochures have appeared. The new numbers more than justify previous statements (AM. JOUR. PHARM., Vol. 81, p. 86) regarding this praiseworthy work. It is without question one of the most meritorious works that has yet appeared in pharmacy. The text is clear and readily understood, the illustrations are both numerous and excellent, and the references to the literature are comprehensive, so that it will be for some years to come the standard reference work in pharmacognosy. The work ought to have a large sale in the United States. It is particularly welcome to teachers and should be in the libraries of all of the colleges and schools of pharmacy, and students should be urged to consult it and use it in connection with their studies and special investigations.

THOMAS S. WIEGAND, PH.M.

With the decease of Thomas S. Wiegand, there passed to the "great majority" another of that group of typical druggists of Philadelphia who, during the last century, aimed by precept and practice to establish pharmacy in America on a scientific and professional basis, and whose efforts have had more than a purely local or passing influence. The practice of our art has been shaped and the entire calling has progressed along the lines laid down by this vanguard of pharmacy.

Thomas Snowden Wiegand was born in Philadelphia, November 9, 1825. He was the son of John Wiegand, the senior member of

the firm of Wiegand and Snowden, manufacturers of instruments and extensive dealers in surgical supplies. His father took an active part in the financial and public affairs of the city and was for many years the president of the Western Saving Fund Society.

At an early age, Thomas was sent to the school kept by Richard W. Green, who was the author of one of the earliest and popular school books on etymology. He next attended the school of James Crowell, who was noted as a teacher of English grammar and arithmetic, and here he received a thorough grounding in these elementary studies. Later he entered the Classical Institute and Preparatory School of Joseph P. Engles and also studied French with a private tutor of that language. He was an apt scholar and availed himself of the advantage of having competent and thorough teachers. He applied himself energetically to his studies, and the avidity with which he acquired knowledge is evidenced by the fact that at thirteen years of age he was declared by his masters to be fitted for entrance into the University of Pennsylvania. A university education was the ambition of his youth, but, just at this time, his father met with a serious financial loss and this privilege was denied him. He never forgot this disappointment to his early plans and ambitions.

At the age of fourteen years he entered the employ of Haskell and Merrick, then engaged in the wholesale drug business on Market Street near Fifth, as an apprentice. He remained with this firm until 1845, and while in their employ he attended the Philadelphia College of Pharmacy and was graduated therefrom in 1844. His thesis was entitled, "An Examination of Aristolochia Reticulata," and it is said to have been largely through his work and writings that the U. S. Pharmacopœia recognized the "Texas" serpentaria as an official source of the drug.

In December, 1845, Thomas S. Wiegand was appointed apothecary to the New York Naval Hospital. This position he held for about two years, and valued highly the association during this time with his chief, the late Dr. W. S. W. Ruschenberger, the surgeon in charge. This was an excellent opportunity for prescription experience and for the development of the pharmaceutical ability and skill of this young apothecary. The sick list at times numbered nearly two hundred and, in addition to compounding the prescriptions, it was his duty to make most of the preparations used in the hospital, as well as many of the medical supplies for the naval vessels fitted out at the port.

While engaged in this hospital service, he prepared an exhibit of chemicals of his own preparation for the 16th Exhibition of Domestic Manufactures held by the Franklin Institute of Philadelphia in 1846. At the same exhibition he showed a design for an apothecary's balance. Both of these exhibits were awarded certificates of merit. This was probably the earliest public demonstration of his ability and indicated the practical trend of his mind and the work of his life.

During his residence in New York, he met Miss Georgiana Maxwell, a lady of education and fine musical talent and a member of a prominent family of French descent who had settled in Brooklyn, whom he wooed and later married.

Returning to Philadelphia, he was employed for a few months with Alfred B. Taylor, at that time an accomplished, scientific pharmacist of the highest reputation. He was then engaged for three years with Frederick Brown, Sr., at the well-known store at the northeast corner of Chestnut and Fifth Streets. Deciding to embark in the retail business for himself, he opened a store at the southeast corner of Fifteenth and Race Streets in 1851. His training, valuable experience, and recognized skill and reputation were recognized by the medical profession and the laity likewise, and he soon established a promising business. When his lease expired he was surprised to learn that his landlord had rented the building over his head to another. This compelled him to purchase the building at the northeast corner of the same streets, make needed alterations, and promptly remove thereto. He remained here for a number of years, closely following his calling and taking an active interest in the scientific and pharmaceutical questions of the time. His health became impaired by close application and confinement to the store, and his physician advised him to give up the retail business. In 1866, disposing of his store, he engaged with the then well-known pharmaceutical manufacturing and wholesale drug firm, Bullock and Crenshaw, his special duty being to superintend their pill factory. This firm was the pioneer in America in the manufacture of sugar coated pills. This form of medication became very popular with physicians, and his skill and the reliability and handsome appearance of the products did much to establish these firmly as acceptable dosage forms for prescriptions. He remained with Bullock and Crenshaw for more than sixteen years.

Although engaged in the manufacturing business and asso-

ciated with the wholesale trade for so long a period, Mr. Wiegand was always interested in dispensing and compounding, and the work and problems of the retail pharmacist always appealed to him, and so, after this extended intermission, he purchased a store near Thirty-eighth and Market Streets and again engaged in the retail business. However, his duties as actuary and librarian of the Philadelphia College of Pharmacy increased so rapidly that in 1885 he disposed of this store and, retiring from active drug business, thereafter devoted his entire time to the needs of the College.

In 1852 he became a member of the Philadelphia College of Pharmacy and in 1855 was elected a trustee. Since then, he has been continuously associated with the work of the College in some official capacity. It is given to but very few indeed to complete more than half of a century associated with the work of one institution. His faithful service in every position in the College that he has been called upon to fill, his sacrifices of time and energy in behalf of his alma mater were no small factors in deciding her progress, and merited our admiration and won our regard.

In 1868, when the College decided to dispose of its first property built on Zane Street and remove to its present site on Tenth Street above Arch Street, he was made secretary of the Committee on Ways and Means and chairman of the Building Committee. He personally made the preliminary sketches for submission to the architect. In 1881, he again served as chairman of the Building Committee under whose supervision the laboratories and rear buildings on Elwyn Street were erected. He also prepared a set of preliminary sketches covering ground plans and outlining the extensive rebuilding of the front and lecture rooms that was done in 1892.

His service on the Committee on Publication of the AMERICAN JOURNAL OF PHARMACY covered a consecutive period of more than twenty-five years, and for at least twenty years of this time he acted as the secretary of that committee.

In 1878 he was elected actuary of the College and in addition served as librarian. For a number of years he devoted only a portion of his time each day to these duties, but by 1885 this work had increased to such an extent that it demanded his entire time. When Wm. C. Bakes who had been secretary of the Board of Trustees for many years died in 1886, the duties of this office were added to those of the actuary. Despite advancing years he acceptably discharged these added labors, until the greatly increased

office work resulting from extension of the instruction and increased number of students compelled the College in 1900 to elect as registrar one who could devote his entire time to the financial and clerical work necessitated. During the remaining years of his life he continued to serve as librarian but was ever ready to give advice or render assistance whenever possible.

When the American Pharmaceutical Association was organized in the Philadelphia College of Pharmacy in 1852, he was greatly interested but, as he had not received a personal invitation to join in the movement, his retiring disposition and natural diffidence prevented his taking part. Nevertheless, he could not resist the temptation to get as near as possible, and in recent years he related how, during these initiatory meetings, he stood on the outside near an open window and greatly enjoyed hearing the older and prominent pharmacists who engaged in the discussions. However, he joined the American Pharmaceutical Association in 1857 and always took a lively interest in its proceedings. For a number of years he served on the Executive Committee and as the secretary penned some of the most able reports presented.

Thomas S. Wiegand was an educated pharmacist and possessed high ideals concerning the proper work and standing of the apothecary. He was a student of pharmaceutical literature and enjoyed correspondence and association with the best men in the calling. His long years of service in the College and in pharmaceutical circles brought him in contact with the most eminent pharmacists, and he appreciated thoroughly their friendship and related many reminiscences of these.

He was a faithful attendant at the pharmaceutical meetings and for many years he was a leading spirit in this part of the College work. Before these meetings were placed in charge of a standing committee, he assumed it to be part of his duty to arrange the programs, issue notices, and as secretary to record the transactions and prepare an account for publication in the AMERICAN JOURNAL OF PHARMACY. He occasionally contributed papers and his verbal communications were numerous and were noticeable because of their practical application to the needs of the druggist.

As a pharmaceutical writer, he adopted a plain style that, without pretence, set forth his views in language that was choice yet easily understood. He was not a prolific writer nor was his name associated with highly scientific investigations, but his contributions

were valuable to the dispensing pharmacist, as they supplied formulas and the applications of scientific and mechanical principles to the daily work of the apothecary. They consist of about fifty papers mostly published in the AMERICAN JOURNAL OF PHARMACY. It was their practicability that made them valuable. His interest in the practice and history of pharmacy never abated, and these were the themes of his conversation and the dreams of his ambition even in the declining days of his life when the infirmities of age robbed him of the energy necessary for action. In a conversation with the writer only a week or two prior to his decease, he still planned to take up some additional work along these lines.

Two editions of Parrish's "Practical Pharmacy" had already appeared and Professor Edward Parrish had commenced the preparation of the third edition when his premature death occurred in September, 1874. In this contingency the publisher, Mr. Henry C. Lea, selected Thomas S. Wiegand as an educated practical pharmacist possessing the requisite standing, reputation, and ability to continue and edit the work. The third edition was published under his editorship and some years later also the fourth edition.

In recognition of his contributions to pharmacy and his services to the advancement of the profession, his Alma Mater conferred upon him the degree of Master in Pharmacy, *honoris causa,* in 1888.

Thomas S. Wiegand always took a very active interest in the work of the Alumni Association of the Philadelphia College of Pharmacy, and throughout the greater portion of its existence served on its Executive Committee. He was elected President of this association in 1865 and his popularity is shown by the fact that he was re-elected to this office for six consecutive terms. This was a pre-eminent and notable honor in an association, which, it is believed, has not since elected a presiding officer for more than one term. For some years prior to his decease he had the distinction of being the oldest alumnus of the College.

It was as actuary of the Philadelphia College of Pharmacy for a period of twenty-two years that probably the most important part of the life work of Thomas S. Wiegand was accomplished. His temperament and his kind and genial disposition peculiarly qualified him for this position. In the performance of his official duties he became acquainted with each matriculant and his many kindly acts endeared him to these embryo pharmacists, and he was looked

up to and esteemed as the students' friend. A word of advice, an explanation of a perplexing problem, a suggestion as to a title for thesis, a reference to pharmaceutical literature, a fatherly admonition to the wayward, a word of encouragement where needed, assistance in securing work or board, and guidance in financial matters were but a few of the hundreds of ways and favors by which he impressed his personality on the students. These kindly offices, though small in themselves, all had their influence and effect in shaping the future career of many of those who have since been successful and become prominent in pharmaceutical circles. Many of these now recall how much they owe to this association and have a sincere warm regard for the memory of that dear spirit of their college attendance whom they reverently and endearingly called "Uncle Thomas." He was the happy medium of communication between the trustees and students and in the performances of his duties he managed to cheer up and stimulate them to their best efforts and won their regard and affection as no other official of the College has yet done.

The same spirit marked his intercourse with his associates, members, visitors, and friends of the College. The courteous gentleman, ever ready to render assistance and to sacrifice himself, was always at their command. He was never more contented nor better satisfied than when performing some kindly service for a friend. His gratification was measured quite as much by his personal satisfaction at being able to render a service as by the gratitude of his friend. His life and character exemplified the words: "In the intercourse of social life, it is by little acts of watchful kindness recurring daily and hourly,—and opportunities of doing kindnesses, if sought for, are forever starting up,—it is by words, by tones, by gestures, by looks, that affection is won and preserved." His qualifications of the heart were as pronounced as those of his mental ability, and so by labors of love he endeared himself to all who came within his influence.

By his devotion to the College he undoubtedly sacrificed his time and opportunity for personal and financial advancement, yet his nature was such that

> "Generous as brave,
> "Affection, kindness the sweet offices
> Of love and duty, were to him as needful
> As his daily bread."

Thomas S. Wiegand possessed a very retentive memory. He often surprised a pharmacist on visiting the College several decades after graduation by recalling his name and those of his class associates along with incidents of their college experience. To a very large degree this faculty was retained by him till the end and accounted for the reminiscent character of his talks on public occasions. Those who were present at the last alumni reunion and banquet will never forget his pathetic appearance and remarks at this his last appearance at a public function.

For several years his many friends have been compelled to note the general inroads of age. His ambition and active mentality sustained him in his determination to participate in the events of this year's commencement week. Since then, the infirmities of old age became more evident and gradually the physical organs lost vitality till exhausted nature ceased the strife.

"Tired he sleeps and life's poor play is o'er."

At the full ripe age of 83 years he departed this life on August 10th and his body was interred on August 14th alongside of those of his wife and daughter in the family plot in the cemetery at Beverly, N. J. He is survived by two daughters.

The correct estimate of his worth and the value of his life cannot be gauged by the usual standards of men. His life was not lived in the public eye, and neither worldly fame, position, nor wealth became his portion. His services were those of a quiet unobtrusive life of devotion, true friendship, and self-sacrifice, and were not marked by conspicuous deeds of valor that called for public plaudit. His contributions to the literature are by no means an adequate measure of his influence on pharmacy. Far more important and greater in achievement has been that quiet influence exerted through his association and the value of his example on students at the period of life when characters are formed and lives moulded.

The historians of the world record the martial events, great discoveries, social advances, literary progress, and political discussions, but such services to humanity as were rendered by the gentle spirit of our departed friend remain unrecorded by these. Pericles said: "For of illustrious men the whole earth is the sepulchre; and not only does the inscription upon the columns in their own land point it out, but in that also which is not their own there dwells with every one an unwritten memorial of the heart, rather than of a material monument."

It is very doubtful if the lives of many of those whom the world has judged to be illustrious have been more fruitful, more beneficial, or exerted a wider influence in shaping the characters and lives of others than has been the quiet humble career of this unassuming pharmacist. It remains for God alone to estimate the worth of such a life and record its true value.

G. M. B.

THE BENZOATE OF SODA CONTROVERSY.

The following is an excerpt from an editorial in *The Outlook* for September 11, 1909, which not only shows how one of the leading lay publications of the country looks at this problem but also furnishes an illustration of how the unscrupulous seek to advance their interests:

"It is true that benzoate of soda is used in some food products of a high grade, not to conceal bad material, but because the manufacturers believe that they can best maintain the natural flavor in this way. But, in view of the past, no one can complain if chemical preservatives are looked upon with suspicion, and, considering the prevailing commercial standards in this country, it appears to us that there is more danger of giving food manufacturers too much latitude than there is of restricting them too much. The controversy over benzoate of soda will at least have served one good purpose if it arouses the country to the need of the most rigorous kind of inspection and regulation of every class of food-producing establishment. In some way the country will insist that only wholesome materials are used, and that hygienic methods of preparing those materials are followed.

"And, finally, the manufacturers who believe sincerely in the right and propriety of their use of benzoate of soda are not really doing their cause good by some of their methods of creating public opinion. An organization bearing the high-sounding title of the National Association for the Promotion of Public Health, and purporting to be a philanthropic and public-spirited society, is really maintained as an advertising or press agency by some at least of the manufacturing group which use benzoate of soda. This press agency recently submitted to *The Outlook* for publication an article by a physician which, under the guise of a charitable appeal for poor children suffering from infantile paralysis, was a thinly disguised advocacy of the use of benzoate of soda in preserved foods."